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CLAIMS

1. An attenuated bacterium in which the native ferric uptake regulation (*fur*) gene, or a functional homologue thereof, is modified such that the expression of the *fur* gene product, or homologue thereof, is regulated independently of the iron concentration in the environment of the bacterium.

2. A bacterium according to claim 1 which is a gram-negative bacterium.

3. A bacterium according to claim 2 which is selected from the group consisting of *Neisseria meningitidis*, *Neisseria gonorrhoeae*, *Helicobacter pylori*, *Salmonella typhi*, *Salmonella typhimurium*, enteropathogenic *E. coli* (EPEC), enteroinvasive *E. coli* (EIEC), enterotoxigenic *E. coli* (ETEC), enterohaemorrhagic *E. coli* (EHEC), verotoxigenic *E. coli* (VTEC), *Vibrio cholerae*, *Shigella spp.*, *Haemophilus influenzae*, *Bordetella pertussis* and *Pseudomonas aeruginosa*.

4. A bacterium according to claim 3 which is selected from *Neisseria meningitidis* and *Neisseria gonorrhoeae*.

5. A bacterium according to any one of the preceding claims which has been attenuated by mutation of a gene essential for the production of a metabolite or catabolite not produced by a human or animal.

6. A bacterium according to any one of the preceding claims which has been attenuated by a mutation of an *aro* gene and/or an *asd*, *pur* or *pyr* gene.

7. A bacterium according to claim 6 wherein said gene is *aroA*, *aroB*, *aroC*, *aroD*, *aroL*, *purA*, *purB*, *purE*, *pyrA*, *pyrB* or *pyrE*.

8. A bacterium according to any one of the preceding claims which further comprises a *recA* mutation.

9. A bacterium according to any one of the preceding claims which further comprises a

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mutation in which expression of a toxin gene has been modified or eliminated.

10. A bacterium according to any one of the preceding claims which further comprises a mutation at a site homologous to the *E. coli minB* locus.

11. A bacterium according to any one of the preceding claims which further comprises a mutation in a gene involved in the uptake of DNA.

12. A bacterium according to claim 11 which is *N. meningitidis* or *N. gonorrhoeae* and wherein the gene involved in the uptake of DNA is *comA*.

13. A bacterium according to any one of the preceding claims which is *N. meningitidis* or *N. gonorrhoeae* and which further comprises a mutation in the *galE* gene.

14. A bacterium according to claim 13 which further comprises a mutation in the *opc* gene to modify or eliminate expression of *opc* protein.

15. An *N. meningitidis* strain which has the genotype: *aroB, lac:fur* fusion, *recA* or *aroB, galE, lac:fur* fusion, *recA*.

16. An *N. meningitidis* strain which has the genotype: *aroL, lac:fur* fusion, *recA* or *aroL, galE, lac:fur* fusion, *recA*.

17. An *N. meningitidis* strain according to claim 15 or 16 which further comprises at least one of a *minB* mutation, an RTX negative phenotype, and an *opc* gene the expression of which has been modified or eliminated.

18. A preparation of membrane vesicles obtained from a bacterium as defined in any one of claims 1 to 17.

19. A vaccine which comprises a bacterium as defined in any one of claims 1 to 17 or a preparation as defined in to claim 18 together with a pharmaceutically acceptable diluent or

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carrier.

20. A vaccine according to claim 19 for use in a method of treatment of the human or animal body.

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21. A method of protecting an individual against a bacterial infection which comprises administering to the individual an effective amount of a bacterium as defined in any one of claims 1 to 17 or a preparation as defined in claim 18.

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22. A process for preparing a vaccine composition comprising an attenuated bacterium as defined in any one of claims 1 to 17 which process comprises:

- (a) inoculating a culture vessel containing a nutrient medium suitable for growth of said bacterium;
- (b) culturing said bacterium;
- (c) recovering bacteria from the culture; and
- (d) mixing said bacteria with a pharmaceutically acceptable diluent or carrier.

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23. A method for producing a bacterium according to claim 1 which method comprises modifying the native *fur* gene, or a functional homologue thereof, of an attenuated bacterium such that expression of said *fur* gene or homologue is regulated independently of the iron concentration in the environment of the bacterium.

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24. A method according to claim 23 wherein said bacterium has been attenuated by at least one mutation as defined in any one of claims 5 to 7.

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